CHAPTER 35
EARLY EFFECTS OF RADIATION

Early Effects of Radiation
- A radiation response in human within a few days to months
- It is described as *deterministic*

Deterministic Radiation Response
- Biologic response whose severity varies with radiation dose
- A dose threshold usually exists

ACUTE RADIATION LETHALITY

Death
- The most devastating human response to radiation exposure

Acute Radiation-Induced Lethality
- It is of only academic interest in diagnostic radiology

PRINCIPAL EARLY EFFECTS OF RADIATION EXPOSURE ON HUMANS & THE APPROXIMATE THRESHOLD DOSE

Effect	Anatomic Site	Threshold Dose
Death	Whole body	200 rad/2 Gy_t
Hematologic depression	Whole body	25 rad/250 mGy_t
Skin erythema	Small field	200 rad/2 Gy_t
Epilation	Small field	300 rad/3 Gy_t
Chromosome aberration	Whole body	5 rad/50 mGy_t
Gonadal dysfunction	Local tissue	10 rad/100 mGy_t

Diagnostic x-ray beams always result in partial-body exposure, which is less harmful than whole-body exposure!

Chernobyl Incident
- April 1986

Three Mile Island Incident
- March 1979

Acute Radiation Syndrome
- Radiation sickness that occurs in human after the whole-body dose s of 1 Gy (100 rad) or more of ionizing radiation delivered over a short time

Three Syndromes
- Hematologic Death, Gastrointestinal (GI) Death & Central Nervous System (CNS) Death

Prodomal Period
- The immediate response of radiation sickness
- *Approximate Dose:* > 100 rad
- *Mean Survival Time:* —
- *Clinical S&S:* nausea, vomiting & diarrhea

Latent Period
- The time after exposure during which there is no sign of radiation sickness
- *Approximate Dose:* 100-10, 000 rad
- *Mean Survival Time:* —
- *Clinical S&S:* none

Hematologic Syndrome
- It is characterized by a reduction in white cells, red cells & platelets
- *Approximate Dose:* 200-1000 rad
- *Mean Survival Time:* 10-60 days
- *Clinical S&S:* nausea, vomiting, diarrhea, anemia, leukopenia, hemorrhage, fever & infection
- *Prodomal Period:* mild symptoms
- *Latent Period:* general feeling of wellness
- *Period of Manifest Illness:* vomiting, mild diarrhea, malaise, lethargy & fever
- *Recovery:* 2-4 weeks or 6 months (full)
- *Cause of Death:* generalized infection, electrolyte imbalance & dehydration

GI Period
- It occurs principally because of severe damage to the cells lining the intestines
- *Approximate Dose:* 1000-5000 rad
- *Mean Survival Time:* 4-10 days

- *Clinical S&S:* same as hematologic plus electrolyte imbalance, lethargy, fatigue & shock
- *Prodomal Period:* vomiting & diarrhea
- *Latent Period:* no symptoms present
- *Period of Manifest Illness:* second wave of nausea & vomiting, followed by diarrhea, anorexia
- *Cause of Death:* unprevented rapid progression of symptoms

CNS Period
- Its ultimate cause is elevated fluid content of the brain
- *Characterized By:* increased intracranial pressure, vasculitis & meningitis
- *Approximate Dose:* > 5000 rad
- *Mean Survival Time:* 0-3 days
- *Clinical S&S:* same as GI plus ataxia, edema, system vasculitis & meningitis
- *Prodomal Period:* severe nausea & vomiting
- *Latent Period:* earlier symptoms disappear
- *Period of Manifest Illness:* more severe prodomal symptoms, disoriented, loss muscle coordination, dyspnea, convulsive seizures, loss of equilibrium, ataxia & lethargy

$LD_{50/60}$
- The dose of radiation to the whole body that causes 50% of irradiated subjects to die within 60 days
- It quantitatively measured the acute radiation lethality
- *Humans:* 350 rad

Acute radiation lethality follows a nonlinear, threshold dose-response relationship!

Mean Survival Time
- Average time between exposure & death
- *Hematologic Syndrome:* dose dependent
- *GI Syndrome:* remain constant
- *CNS Syndrome:* dose dependent

LOCAL TISSUE DAMAGE

Local Tissue Damage
- It follows a threshold-type dose response relationship
- *Characteristic:* deterministic response

Local Tissues That Can Be Affected Immediately
- Skin
- Gonads
- Bone marrow

Partial-Body Irradiation
- A higher dose is required to produce a response
- It affects organ & tissue
- *Effect:* cell death
    - *Result:* shrinkage of the organ or tissue

Atrophy
- The shrinkage of an organ or tissue due to cell death

EFFECT ON SKIN

Skin
- The tissue with which we have had the most experience
- Three Layers
    - *Epidermis:* outer layer
        - *Basal Cells:* its lowest layer
    - *Dermis:* intermediate layer of connective tissue
    - *Subcutaneous:* layer of fat & connective tissue
- *Other Accessory Structures:* hair follicles, sweat glands & sensory receptors
- *Cells Replacement Rate:* 2 %/day (50 % for GI)
- *Skin Effects:* nonlinear, threshold dose-response relationship

Basal Cells
- The stem cells that mature as they migrate to the surface of the epidermis

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Damage to basal cells results in the earliest manifestation of radiation injury to the skin!

Orthovoltage X-rays
- *Range:* 200-300 kVp

Erythema
- A sunburn-like reddening of the skin
- The first observed biologic response to radiation exposure

Desquamation
- Ulceration & denudation of the skin

Moist Desquamation
- The clinical intolerance for radiation therapy

X-ray-Induced Erythema
- One of the hazards to the patient the early of radiology

Skin-Erythema Dose (SED)
- Dose of radiation, usually about 200 rad, that causes redness of the skin

Epilation/Alopecia/Fox Mange
- Loss of hair

SED_{50}
- The dose required to affect 50% of those irradiated
- *Dose:* 500 rad

POTENTIAL RADIATION RESPONSES OF SKIN FROM HIGH-DOSE FLUOROSCOPY

Potential Radiation Response	Threshold Dose	Approximate Time of Onset
Early transient erythema	200 rad	Hours
Main erythema	600 rad	10 days
Temporary epilation	300 rad	3 weeks
Permanent epilation	700 rad	3 weeks
Moist desquamation	1500 rad	4 weeks

Grenz Rays
- It is used to treat tinea capitis (ringworm)
- *Range:* 10-20 kVp

EFFECTS ON GONADS

Testes
- The male gonads
- It produces *spermatogonia* & matures into *sperm*

Ovaries
- The female gonads
- It produces *oogonia* & matures into *ovum*

Germ Cells
- Produced by both ovaries & testes

Gametogenesis
- The process of development of germ cells

Progression of Germ Cell
- *Male:* Spermatoginia (most radiosensitive) → Spermatocyte → Spermatid → Sperm
- *Female:* Primordial Follicle → Mature Follicle (most radiosensitive) → Corpus Letuem → Ovum

Oogonia
- The stem cells of the ovaries
- They multiply in number only before birth & during fetal life

Primordial Follicles
- They grow to encapsulate the oogonia

Oocyte
- A matured oogonia

Ovum
- A mature female germ cell
- *Fertilization:* 400-500 ova
    - Number of years of menstruation times 13 per year

Spermatogonia
- The stem cells of the testes
- Continually being produced from stem cells progressively through a number of stage to maturity

Spermatocyte
- A matured spermatogonia

Spermatid
- A matured spermatocyte

Spermatozoa/Sperm
- A mature male germ cell
- *Maturation Process:* 3-5 weeks

Ovaries
- Irradiation Causes
  - *Early Life:* atrophy
  - *After Puberty:* suppression & delay of menstruation
- *10 rad:* suppresses menstruation
- *25-50 rad:* increased genetic mutations
- *200 rad:* temporary sterility
- *500 rad:* sterility

The most radiosensitive cell during female germ cell development is the oocyte in the mature follicle!

Testes
- *Irradiation Causes:* atrophy
- *10 rad:* reduce the number of spermatozoa
- *200 rad:* temporary sterility
- *500 rad:* sterility

Spermatogonial Stem Cells
- The most sensitive phase in the gametogenesis of the spermatozoa

Male Gametogenesis
- A self-renewing system

HEMATOLOGIC EFFECTS

Periodic Blood Examination
- The only monitoring performed on x-ray & radium workers before
- Total cell counts & a white cell differential count

Under no circumstances is a periodic blood examination recommended as a feature of any current radiation protection program!

Hematologic Depression
- *Threshold Dose:* 25 rad

Hemopoietic System
- Another example of cell renewal system
  - Same with gametogenesis
- Bone marrow
- Circulating blood
- Lymphoid tissue
  - Lymph nodes, Spleen & Thymus
- *Principal Effect of Radiation:*
  - Depressed number of blood cells in the peripheral circulation

Pluripotential Stem Cell
- Stem cell that has the ability to develop into several different types of mature cells
- It produces lymphocytes, granulocytes, thrombocytes & erythrocyte

Lymphocytes/White Blood Cells
- Blood cells involved in the immune response
- Manufactured by spleen & thymus
- *Lifetime in the Bone Marrow:* varying (hours or years)
- *Lifetime in the Peripheral Blood:* varying (hours or years)

Granulocytes
- Scavenger type of cells used to fight bacteria
- *Lifetime in the Bone Marrow:* 8-10 days
- *Lifetime in the Peripheral Blood:* couple of days

- *Recovery:* 2 months

Thrombocytes/Platelets
- Blood cells involved in the clotting of blood to prevent hemorrhage
- *Lifetime in the Bone Marrow:* 5 days
- *Lifetime in the Peripheral Blood:* 1 week
- *Recovery:* 2 months

Erythrocytes/Red Blood Cells
- Blood cells that are transportation agents for oxygen
- Less sensitive than the other blood cells
  - *Rationale:* long lifetime in the peripheral blood
- *Lifetime in the Bone Marrow:* 8-10 days
- *Lifetime in the Peripheral Blood:* 4 months
- *Recovery:* 6 months to 1 year

Bone Marrow
- It manufactures most circulating blood cells including lymphocytes
- *Child:* uniformly distributed throughout the skeleton
- *Adult:* restricted to flat bones such as ribs, sternum, skull & ends of long bones

HEMOPOIETIC CELL SURVIVAL

Principal Radiation Response of Hemopoietic System
- Decrease in the number of all types of blood cells in the circulating peripheral blood

Lethal Injury
- It causes depletion of mature circulating cells

Lymphopenia
- Reduced in number of lymphocytes

The lymphocytes & the spermatogonia are the most radiosensitive cells in the body!

Granulocytosis
- Rapid rise in number of granulocytes

Granucytopenia
- Rapid decrease & slower decrease of granulocytes

Thrombocytopenia
- Depletion of platelets

CYTOGENETIC EFFECTS

Cytogenetics
- The study of the genetics of cells particularly cell chromosomes

Radiation-induced chromosome aberrations follow a nonthreshold dose-response relationship!

Human Peripheral Lymphocytes
- Most often used for cytogenetic analysis

Karyotype
- A chromosome map

Each cell consists of 22 pairs of autosomes & a pair of sex chromosomes – the X-chromosomes from the female & the Y chromosomes from the male!

Chromosomes Structural Radiation Damage
- Single-Hit Chromosome Aberrations
- Double-Hit Chromosome Aberrations

Reciprocal Translocation
- It requires a karyotype for detection

Point Genetic Mutations
- Undetectable even with karyotype construction

Hit
- Radiation interaction with chromosomes

DNA Hit
- It results in an invisible disruption of the molecular structure of the DNA

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Chromosome Hit
- It produces a visible derangement of the chromosome
- It represents severe damage to the DNA

Singe-Hit Chromosome Aberration
- Visualized & recorded during the M phase
- Irradiation During G_1 Phase
  - *Cause:* chromatid break
  - *During S Phase:* replicated
  - *During Metaphase:* a chromosome with material missing from the ends of two sister chromatids & two acentric fragments
- Irradiation During G_2 Phase
  - *Causes:* single or double chromatid break
  - *During S Phase:* replicated
  - *During Metaphase:* a chromosome with an arm that is obviously missing genetic material & a chromatid fragment

Chromatid Deletion
- The breakage of a chromatid

Isochromatid
- Fragments in chromosome aberrations

Acentric
- Without a centromere

Multi-Hit Chromosome Aberration
- Not uncommon
- Irradiation During G_1 Phase
  - *Causes:* ring & dicentric chromosomes
  - *Ring:* when two hits occur on the same chromosome
  - *Dicentric:* when adjacent chromosome each suffer one hit & recombine
- *Irradiation During G_2 Phase:* similar to G1 phase but rarer

Stickiness
- A condition in which the mechanism for the joining of chromatids depends

Radiation-Induced Reciprocal Translocation
- Multi-hit chromosome that require karyotype analysis for detection
- *Results in:*
  - No loss of genetic material
  - Simply a rearrangement of the genes

Kinetics of Chromosome Aberration
- *Single-Hit Aberration:*
  - It occurs at very low doses of radiation
  - *Dose-Response Relationship:* linear, nonthreshold
- *Multi-Hit Aberration:*
  - It occurs when the radiation dose exceeds approximately 100 rad
  - *Dose-Response Relationship:* nonlinear, nonthreshold

Radiation Dose-Response Relationship For Cytogenetic Damage
- *Single-Hit:* $Y = a + bD$
- *Multi-Hit:* $Y = a + bD + cD2$

Cytogenetic Analysis
- Biologic radiation dosimeter

Approximate Chromosome Aberration Frequency
- Two single-hit aberrations per rad per 1000 cells
- One multi-hit aberration per 10 rad per 1000 cells